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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/856,422	12/13/2001	Zvi Kam	U013475-2	7739
140	7590	09/06/2005	EXAMINER WERNER, BRIAN P	
LADAS & PARRY 26 WEST 61ST STREET NEW YORK, NY 10023			ART UNIT 2621	PAPER NUMBER

DATE MAILED: 09/06/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/856,422

Applicant(s)

KAM, ZVI

Examiner

Brian P. Werner

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 22 February 2005.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 34,35 and 38-41 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 34,35 and 38-41 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 22 February 2005 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____

DETAILED ACTION

Priority

1. This application is a national stage application of PCT/IL99/00645 filed on November 30, 1999, which claims priority to Israel application 127359, filed on December 1, 1998.

Response to Amendment

2. The following Office Action is responsive to the amendment received on February 22, 2005. Claims 34, 35 and 38-41 are currently pending.

Drawings

3. The drawing corrections received on February 22, 2005 are accepted.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 38 and 39 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with

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which it is most nearly connected, to make and/or use the invention. Claim 38, which is representative of claim 39, will be exemplified.

Claim 38 requires:

an adaptive optics controller to control and adaptive optical element in a confocal microscope to correct aberrations resulting from variations in the refractive index at a multiplicity of locations in a medium; where

the adaptive optics controller uses an abberated wavefront determined by the ray tracer.

The entirety of the specification is directed to correcting aberrations resulting from refractive index variations using image processing. For example, refer to figure 2, numeral 34, figure 3, numeral 54 and figure 7. That is, in order to correct the aberrations, a location dependent point spread function is convoluted with an observed image as depicted at figure 3, numeral 54. This is a mathematical manipulation and reconstruction.

However, claim 38 requires a physical, or optical element to be placed in the optical path of a confocal microscope which is adaptive and utilizes "said abberated wavefront" to "correct aberrations resulting from the variations in the refractive index". The adaptive optical element that performs this process, and the manner of controlling the adaptive optical element is not sufficiently described by the specification to enable one skilled in the art to make and use the invention without undue experimentation.

The only description of this embodiment in the specification is at page 9, in the summary section. Essentially, page 9 describes "an adaptive optical element" in the same manner as

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claimed. Also, page 9 states, "... a method for adding (computationally or physically) in the imaging path a three-dimensional medium (anti-sample) with refractive properties that correct for the distortions of the three-dimensional sample." However, the specification fails to describe what an "anti-sample" is, what it is constructed of, how it works, etc. Because this appears to be a critical aspect of the invention which is necessary for one to make and use the invention, and because there are no known examples of such adaptive anti-samples that utilize an aberrated wavefront for correcting variations of a refractive index in a confocal microscope, one skilled in the art would require more information. **What is the adaptive optical element, how it is made, how does it work, how does it adapt itself, how does change itself to correct for refractive index variations in a sample, how does it utilize an aberrated wavefront, etc.?** At least some of this information would be required for one skill in the art to make and use the invention without undue experimentation. Without any known prior art to start with, one skill in the art would be starting with the suggestions at specification page 9, which is insufficient.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 38 and 39 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Both of these claims require a "confocal microscope". However, claims 34 and 35 from which claims 38 and 39 depend, require one of three types of microscopes ("DIC", "phase" or "fluorescence"), none of which are claimed as being "confocal". Therefore,

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the scope of claims 38 and 39 does not fall within the scopes of the claim from which they depend. Thus, it is unclear what type of microscope is actually required by claims 38 and 39.

Clarification is required.

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

8. Claims 40, which is representative of claim 41, are rejected under 35 U.S.C. 103(a) as being unpatentable over the combination of Goldstein (US 4,827,125 A) and Chan et al. (US 6,275,726 B1).

Goldstein discloses providing a confocal microscope (figure 1; “confocal ... microscope” at column 4, line 37) having an imaging path between a three-dimensional sample (figure 1, numeral 27; “specimen” at column 8, line 6) and its output image plane (figure 1, numeral 35).

Goldstein does not teach:

determining variations of the refractive index in said three-dimensional sample; and
disposing in said imaging path a three-dimensional medium having properties that correct aberrations resulting from said variations of the refractive index in the three-dimensional sample.

Chan teaches imaging a specimen with a confocal microscope (“confocal” at column 2, line 30 and “confocal microscopy” at column 8, line 58), comprising:

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determining variations of the refractive index in said three-dimensional sample (“highly light scattering because of the refractive index (n) variations among water and various inter/intra cellular components ...” at column 1, lines 25-35); and

disposing in said imaging path a three-dimensional medium (“index matching the cellular components” at column 2, line 37; “replacing inter and/or intrastitial (extracellular) fluid with another (replacement) fluid that has a refractive index more similar to that of the inter/intra cellular components” at column 2, lines 63-66) having properties that correct aberrations resulting from said variations of the refractive index in the three-dimensional sample (“enhancing the visualization of turbid biological tissue comprising the reduction of light reflection and refraction” at column 3, lines 29-31; “improves the imaging of tissues” and “improve the depth of penetration and increases signal to noise values” at column 8, lines 55-57).

It would have been obvious at the time the invention was made to one of ordinary skill in the art to dispose the index matching fluid of Chan into the specimen of Goldstein, in order to enhance “the visualization of turbid biological tissue comprising the reduction of light reflection and refraction” (Chan at column 3, lines 29-31), thereby improving “the imaging of tissues” and “the depth of penetration” and increasing “signal to noise values” (Chan at column 8, lines 55-57).

9. Claim 34, which is representative of claim 35, are rejected under 35 U.S.C. 103(a) as being unpatentable over the combination of Presby (US 4,362,943 A) and Schoen (Ray Tracing Analysis for Media with Nonhomogeneous Indices of Refraction).

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Presby discloses an information acquirer (“microscopes” at column 3, line 57) providing information relating to local index variations at any multiplicity of three dimensional locations (“index profile” at column 1, line 57; “refractive index profile” at column 1, line 8) in a medium (“optical fibers” at column 1, line 57), the refractive index variations being determined by fluorescence microscopy (“induced fluorescence” at column 2, line 60; “microscopes are used for ... observing the resulting fluorescence” at column 3, line 58).

While Presby teaches that an “accurate knowledge of the fiber profile is necessary in order to assess the fiber’s transmission properties” at column 1, line 23, Presby does not teach the additional claimed step of:

a computer employing an analytically determined path of a ray through the multiplicity of 3D locations in the medium, for a plurality of rays impinging thereon in different directions, by utilizing the local variations of the refractive index at the multiplicity of 3D locations.

Schoen teaches

a computer program (“computer code” in the abstract) employing an analytically determined path of a ray through the multiplicity of 3D locations in a medium, for a plurality of rays impinging thereon in different directions, by utilizing the local variations of the refractive index at the multiplicity of 3D locations (“to determine ray trajectories in media with spatially varying indices of refractions” in the abstract).

Schoen teaches applications in “fiber-optics” (see the abstract, and section I) for characterizing “the expected system performance” (section I).

It would have been obvious at the time the invention was made to one of ordinary skill in the art to incorporate the ray tracing algorithm of Schoen, utilizing the index profile acquired by

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Presby and as a final step in the assessing of the “fiber’s transmission properties” (Presby, column 1, line 23), in order to “characterize the expected system performance” (Schoen, section I) thereby ensuring that the fiber optics produced by Presby are manufactured exactly to specification and will perform as expected.

Response to Arguments

10. Each of the remarks and/or arguments filed with the aforementioned amendment have been considered:

Claim 112 rejections:

Summary of Applicant’s Remarks:

“The applicants respectfully submit that many kinds of such adaptive optics elements are well known to one of skill in the art, such as are described in the book by R.K. Tyson entitled “principles of Adaptive Optics”, Academic Press, New York, 1991, which is referenced in the Background section of the application. Such elements do not therefore need further elaboration in order to enable the claim.” (applicant’s response not page or paragraph numbered).

Examiner’s Response:

In the 35 U.S.C. 112 rejection, the examiner is not questioning whether adaptive optics are well known. Rather, the question is whether adaptive optics correcting “aberrations” resulting from “variations in the refractive index” are known; especially the control of such

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adaptive optics UTILIZING an “abberated wavefront” derived from tracing “rays”. That is, claim 38 requires determining an abberated wavefront from a plurality of traced rays, and then controlling an adaptive optical element utilizing the abberated wavefront to correct for variations in the refractive index of the sample.

Turning to the R.K. Tyson article, the examiner agrees that adaptive optics are known. However, the question is what the “known” adaptive optics correct for, and what they are responsive to. Tyson states that “adaptive optics ... can change the effects of an optical system by adding, removing, or altering optical elements” at section 1.3. The examiner has no doubt that optical elements, such as filters, lenses, etc. can be adaptively inserted and removed from the optical field. Tyson further states at section 1.3 that “we cannot get rid of diffractive effects; they are inherent in Maxwell’s laws” but “when mechanical or thermal effects degrade the image or propagation process beyond the diffraction limit, we can try to alter the optical system to compensate for the defects even though we cannot get rid of them”.

In summary, Tyson teaches:

- Utilizing adaptive optics to compensate for diffractive effects;
- That diffractive effects cannot be gotten rid of;
- One can merely “compensate” for mechanical and thermal defects.

Tyson DOES NOT teach:

- An adaptive optical element that corrects for variations in the refractive index of the sample; and

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- An adaptive optical element that utilizes an aberrated wavefront to correct for the variations in the refractive index of the sample.

In order for the applicant to rely upon the Tyson reference as evidence of well known subject matter in support of enablement, Tyson would have to teach at a minimum an adaptive optical element that corrects for variations in the refractive index of the sample. In addition, Tyson would also have to teach how the adaptive optical element is responsive to an aberrated wavefront to correct for the variations in the refractive index of the sample. Tyson teaches neither of these elements.

Summary of Applicant's Arguments:

"Examples of such adaptive optical elements include spatial light modulators, which generate a spatially variable phase shift to the wavefront passing therethrough, such as programmable deformable mirrors, pixelated liquid crystal arrays, or an "anti-sample", which is no more than such an adaptive optical element programmed to correct the phase of light passing through the element in order to compensate for the aberrations generated during the passage of the light through the sample" (applicant's response not page or paragraph numbered).

Examiner's Response:

Spatial light modulators, deformable mirrors, pixelated liquid crystal arrays, and anti-samples are not explicitly taught by Tyson, they are not mentioned in the applicant's specification, and they are not of record in any of the references cited by the applicant or

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incorporated by reference into the applicant's specification. Furthermore, even if for example a spatial light modulator was exemplified by Tyson as a type of adaptive optical element, Tyson still would not be teaching the use of that spatial light modulator for correcting variations in the refractive index of a sample either alone, or in response to an aberrated wavefront.

Summary of Applicant's Remarks:

““The nature of what such an adaptive optical element is, including how it is made, how does it work, how does it adapt itself, and how does it changes itself to correct for refractive index variations in the sample, etc” as questioned by the Examiner, are thus known in the art and do not require further explanation” (applicant's response not page or paragraph numbered).

Examiner's Response:

Applicant has pointed to the Tyson reference as demonstrating that adaptive optics are “known”. However, the Tyson reference, as described above, DOES NOT teach the correction of “index variations in a sample” using adaptive optics; and in particular where the adaptive optics are response to an aberrated wavefront.

In summary, and whether the Tyson reference is considered or not, applicant has NOT provided any objective evidence whatsoever that it is known to correct for “index variations in a sample” using adaptive optics; and in particular where the adaptive optics are response to an aberrated wavefront. The applicant's specification is devoid of these details. Nowhere, other than broad statements made in the Summary section of the specification, does the applicant's specification describe how an adaptive optical element is controlled to correct for aberrations

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resulting from the variations in the refractive index of a sample. Nowhere does the specification describe how the adaptive optical element is controlled using an aberrated wavefront. The prior art of record does not make clear that this is well known. In the absence of any other objective evidence teaching these concepts, that the examiner maintains that one skilled in the art would have required undue experimentation to make and use the claimed invention.

Prior Art Rejections – Claims 40 and 41:

Summary of Applicant's Remarks: "However, to the best of the applicants' understanding, nowhere in Chan et al is there mentioned or suggested any determination of the refractive index of the sample" (applicant's response not page or paragraph numbered).

Examiner's Response: Chan, at column 1, lines 25-32, states:

"The refractive index of water is 1.33 while many cellular components have higher refractive indices. For instance, melanin has a refractive index of 1.7 (Vitkin et al., 1994), nucleus has a refractive index of 1.36 Hiramoto, 1979) and dehydrated collagen has a refractive index of 1.53 (Wang et al., 1996)."

Thus, Chan teaches the determination of the refractive indices of various materials that will be viewed under a microscope. It is apparent that Chen has determined several refractive indices by reference to other prior art (i.e., "Vitkin et al.", "Hiramoto", "Wang"). The claim does not clarify how the determination is undertaken.

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Summary of Applicant's Remarks: "The Chan et al. invention relies on the values of refractive index of the various components known in advance, and is in no way concerned with the determination of these refractive indices" (applicant's response not page or paragraph numbered).

Examiner's Response: The claim does not require any particular determination method. The refractive indices of the materials identified by Chan had to be determined by someone, at some time. Chan determines them by pointing to references (e.g., "melanin has a refractive index of 1.7 (Vitkin et al., 1994)" at Chan column 1, line 29). The claim does not require any particular method for determining the refractive indices, or any particular temporal order. Chan meets the broad requirements of the claim as presently recited.

Summary of Applicant's Remarks: "Additionally, to the best of the applicants' understanding, nowhere in Chan et al is there mentioned or suggested disposing a three-dimensional medium in the imaging path between the sample and its output image plane. In the Chan et al patent, the three dimensional refractive index corrective medium is disposed within the sample itself, and not in the above described imaging path" (applicant's response not page or paragraph numbered).

Examiner's Response: The sample is imaged by Chan, and thus the sample itself is in the imaging path. Therefore, given that the 3D refractive index corrective medium disclosed by Chan is deposited in the sample itself, then it too is in the imaging path.

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The remainder of applicant's arguments with respect to the prior art rejections of claims 34 and 35 are moot in view of the new grounds of rejection advanced herein, and necessitated by the amendment.

Conclusion

11. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

Wolleschensky et al. (US 6,771,417 B1) is pertinent as teaching adaptive optics to correct for indices of refraction in a sample (column 1, lines 10-19 and 60-68, column 2, lines 7-15 and 30-33, column 3, line 58, column 4, lines 1-4, column 7, lines 55-62, column 8, lines 3-33 and lines 58-62). Wolleschensky does not however teach the refraction determination and ray tracing of claims 34 and 35. Wolleschensky does however teach the limitations of claims 40 and 41.

12. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37

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CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian P. Werner whose telephone number is 571-272-7401. The examiner can normally be reached on M-F, 8:00 - 4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Mancuso can be reached on 571-272-7695. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Brian Werner
Primary Examiner
Art Unit 2621



BRIAN WERNER
PRIMARY EXAMINER